UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,842	12/07/2001	Jian Ni	1488.131000A	4105

28730 7590 12/23/2003

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
KAUFMAN, CLAIRE M	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,842	NI ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-179* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *62-72 and 117-126* is/are allowed.

6)☒ Claim(s) *35-61,73-116 and 127-179* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11/02, 4/4/02, 12/11/02, 5/30/03
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Inventorship

In view of the papers filed 12/07/01, the inventorship in this nonprovisional application has been changed by the deletion of Jeffery Su.

Claim Interpretation

For claims drawn to "An isolated polypeptide comprising an amino acid sequence...", the specification appears to intend that the amino acid sequence is contiguous, but the polypeptide may include additional amino acid sequence on either end of said an amino acid sequence (*e.g.*, two paragraphs beginning line 28 of page 26). With this interpretation, the splice variant receptor of Rauch et al. (US Patent 6,072,047) which is identical to SEQ ID NO:2 of the instant application with the exception of a 29 amino acid insert, would not qualify as a polypeptide comprising an amino acid sequence identical to SEQ ID NO:2 because the insert occurs within SEQ ID NO:2 of the instant application (after amino acid 131). Nor would a polypeptide comprising amino acids 1 to 133 of SEQ ID NO:2 (claim 160 of the instant application) because the insert of Rauch et al. occurs within the designated fragment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 134-135, 137-144 and 146-151 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising at least 30 contiguous amino acids of amino acids 158-136 of SEQ ID NO:2, does not reasonably provide enablement for a polypeptide comprising an amino acid sequence at least 90% identical to at least 30 contiguous amino acids of amino acids 158-136 of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification discloses SEQ ID NO:2 as a receptor that binds TRAIL and induces apoptosis. Fragment 158-360 is the intracellular domain which contains the death domain (p. 6, lines 1-12). The claims are drawn to a polypeptide comprising an amino acid sequence at least 90% identical to 30 (claim 134) or 50 (claim 143) contiguous amino acids of amino acid 158-360 of SEQ ID NO:2. For claim 134, the 30 contiguous amino acids must bind an antibody with specificity for the polypeptide consisting of amino acids 1-360 of SEQ ID NO:2. This function does not extend to the claimed polypeptide, but only to the fragment of SEQ ID NO:2. While one skilled in the art could use a fragment of SEQ ID NO:2 to produce antibodies for the isolation or localization of the polypeptide of SEQ ID NO:2, one could not predict if a polypeptide 90% or 95% identical to a 30 or 50 amino acid long fragment of amino acids 158-360 of SEQ ID NO:2 could produce an antibody that would also bind SEQ ID NO:2 with enough specificity to be useful for isolation or localization of that disclose receptor protein. Nor does that polypeptide or fragment necessary comprise the death domain or have any known function on its own. The specification does not provide guidance for or examples of using a small polypeptide which shares only some identity with a fragment of SEQ ID NO:2 but does not share a recognized function. It would require undue experimentation to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 35, 36, 38, 39, 43-45, 47, 48, 52-54, 56, 57, 61, 73-77, 81-85, 89-94, 98-100, 102, 103, 107-109, 111, 112, 116, 127-129, 133-138, 142-147, 151-155, 159, 168-174, 178 and 179 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,072,047 (AK1, cited by Applicants).

US Patent No. 6, 072,047 receives priority back to March 12, 1997 (application number 08/815,255) for the TRAIL-R that was isolated from human Jurkat cells and human PS-1 cells. The mature protein comprising the fragment had been purified by affinity purification with TRAIL (TNF-Related Apoptosis-Inducing Ligand; EXAMPLE 1 and 2). The amino acid sequence of the full-length receptor is identical to SEQ ID NO:2 of the instant application with the exception of a 29 amino acid insert beginning after position 131. The amino acid sequence of the fragment of the receptor appears in Figure 1 of the patent, which is the same as amino acids 336-386 of SEQ ID NO:2 of the patent. This TRAIL receptor fragment is identical to amino acids 256-306 of SEQ ID NO:2 of the instant application. As later shown in US Patent 6,072,047, the above fragment functions within a mature DR5 to induce apoptosis. The polypeptide produced by Jurkat cells would reasonably be expected to be the same as that produced by a recombinant eukaryotic cells in terms of sequence and glycosylation, absent evidence to the contrary. The polypeptide would necessarily have had to have been in a carrier (*i.e.,* buffer) for tryptic digest.

Note that because of the open language of the claims reciting "comprising", such as in claim172, the claims read on the full-length protein of the patent. This is also true for claims such as claim 73 with functional limitations of substitution of a fragment into a DR5 variant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered

therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 40-42, 49-51, 58-60, 78-80, 86-88, 95-97, 104-106, 113-115, 130-132, 139-141, 148-150, 156-158 and 175-177 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,072,047.

US Patent No. 6, 072,047 is relied on for the teachings set forth above.

The patent also teaches methods and means for recombinant expression of the protein: "A method of producing TRAIL-R polypeptides comprising culturing host cells transformed with a recombinant expression vector encoding TRAIL-R, under conditions that promote expression of TRAIL-R, then recovering the expressed TRAIL-R polypeptides from cultures." (col. 8, lines 6-22). The sequence of a fragment of the TRAIL-R shown in Figure 1 is identical to amino acids 256-306 of SEQ ID NO:2 of the instant application. The DNA fragment was obtained by using degenerate oligonucleotide primers for PCR (EXAMPLE 3). The encoding DNA may be operably linked to a suitable regulatory sequence (col. 8, lines 23-40). Also taught is how to make a polynucleotide encoding fusion protein of TRAIL-R and human Ig Fc region fusion protein in order to make TRAIL-R dimers (col. 13, lines 3—35). Such dimers are useful for "facile purification by affinity chromatography over Protein A or Protein G columns" (col. 14, lines 9-14 and col. 15, lines 16-22). TRAIL receptors binds TRAIL, which had been demonstrated to induce apoptosis in some cancer cells as well as virally infected cells (col. 1, lines 15-22). US Patent No. 6,072,047 does not teach the protein comprising a heterologous polypeptide.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a fusion polypeptide comprising TRAIL-R and a heterologous polypeptide, including a human Ig Fc domain. It would have been obvious to make a polynucleotide comprising the TRAIL-R DNA fragment operably linked to a heterologous regulatory sequence as well as a heterologous polynucleotide sequence that encoded a human Ig Fc domain, and a method of making such, as taught by US Patent No. 6,072,047 for well known and suggested purposes of DNA amplification and protein production and purification. Because the DNA fragment of Figure 1 had been identified as encoding part of a TRAIL receptor, one would have

been motivated to produce the above described products to characterize aspects of the receptor that binds TRAIL ligand, which was known to be involved in apoptosis and have clinical implications. Alternatively, with the knowledge that was well known of the degeneracy of the genetic code, one of ordinary skill in the art could have readily envisioned all degenerate sequences that encoded the TRAIL-R protein without knowing what the actual native sequence was. This knowledge was the basis of making the degenerate oligo primers of US Patent 6,072,047 that allowed TRAIL-R DNA to be obtained. One would have been motivated to produce the above described mature TRAIL-R fused to a heterologous polypeptide to characterize aspects of the receptor that binds TRAIL ligand, which was known to be involved in apoptosis and have clinical implications.

Art of Record

Applicants have made US Patent 6,342,369 of record in IDS paper filed 4/4/02. This patent is not available as prior art. It is also noted that amino acid 32 is different between SEQ ID NO:1 of the patent and SEQ ID NO:2 the instant application. US Patent 6,313,269, also made of record in the same IDS, receives benefit for effective filing date of Provisional Application 60/041,230, filed 3/14/97, which teaches amino acids 58 to 360 of SEQ ID NO:2 of the instant application. While this patent is available as prior art, it is cumulative with that already relied upon. Additionally, it is noted that amino acid 106 (called amino acid 55 in the instant application) is different between SEQ ID NO:2 of the patent and the instant application. The species claimed in the patents are not obvious in light of the instant claims.

Conclusion

Claims 62-72 and 117-126 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791 (changing to (571)272-0873 on 01/23/04). Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564 (changing to (571)272-0871 on 01/23/04).

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 872-9306. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

December 18, 2003